Remarks

Status of the Claims and Support for the Amendments to the Claims

By the foregoing amendments, claims 13-16 and 20 have been canceled. Claims 1-6, 9 and 11 are sought to be amended. New claims 22-43 are sought to be added. Support for the amendments to claims 1-6, 9 and 11, and for new claims 22-43, can be found throughout the specification, and in the claims as originally filed. Therefore, these amendments introduce no new matter. Upon entry of the foregoing amendments, claims 1-12, 17-19 and 21-43 are pending in the application, with claims 1, 4, 5, 9, 34 and 39 being the independent claims. Claims 6, 10, 17 and 19 have been withdrawn from consideration by the Examiner.

Summary of the Office Action

In the Office Action dated October 2, 2007, the Examiner has made five objections to the claims, and four rejections of the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Objections to the Claims

In the Office Action at pages 2-3, Sections 2-4, the Examiner has objected to claims 4, 5, 7-9 and 11-12. Claims 4, 5 and 9 are objected to for allegedly failing to further limit the subject matter of a previous claim. Claim 11 is objected to as being of improper form. Claims 7, 8 and 12 are objected to for depending from a rejected base claim. Applicants respectfully traverse these objections.

With regard to the objection to claims 4, 5 and 9, Applicants respectfully disagree with the Examiner's objections. However, solely to expedite prosecution, and not in acquiescence to these objections, present claims 4, 5, and 9 have been re-written as independent claims. Hence, these objections have been overcome.

With regard to the objection to claim 11, present claim 11 depends only from claim 9, an independent claim. Hence, the objection to claim 11 has been overcome.

With regard to the Examiner's objection to claims 7, 8 and 12, Applicants respectfully submit that the base claims from which these claims depend are allowable. Hence, this objection has been overcome.

In view of the foregoing remarks, Applicants respectfully request that the objections to claims 4, 5, 7-9 and 11-12 be reconsidered and withdrawn.

The Rejection Under 35 U.S.C. § 101

In the Office Action at pages 3-4, section 5, the Examiner has rejected claims 1-5 and 9 under 35 U.S.C. § 101, as allegedly being directed to non-statutory subject matter. Applicants respectfully traverse this rejection.

The Examiner alleges that the claims read on nucleic acids and proteins per se which are found in nature and thus, are unpatentable. Present claims 1-5 recite "isolated nucleic acid" and "isolated DNA." Similarly, present claim 9 recites "isolated Mirafiori lettuce virus coat protein." Applicants respectfully submit that such nucleic acids and proteins not found in nature, and hence, represent statutory subject matter. Therefore, in view of the foregoing remarks, reconsideration and withdrawal of the rejection under 35 U.S.C. § 101 are respectfully requested.

The Rejection under 35 U.S.C. § 112, Second Paragraph

In the Office Action at page 4, section 6, the Examiner has rejected claims 15 and 20 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicants respectfully traverse this rejection.

The Examiner contends that claim 15, and hence claim 20 that depends therefrom, is indefinite because it is unclear if the progeny comprises the nucleic acid encoding the MiLV coat protein, the DNA or the vector.

Applicants respectfully submit that claim 15 is not indefinite. Present claim 22 (which is based on claim 15 as previously presented) recites a transformed plant cell which carries the nucleic acid according to claim 1, the DNA according to any one of claims 4 through 6, or the vector according to any one of claims 7, 12, 18 or 19. Hence, Applicants respectfully submit that this claim is not indefinite. In view of the foregoing remarks, reconsideration and withdrawal of the rejection of claims 15 and 20 are respectfully requested.

The Rejection under 35 U.S.C. § 112, First Paragraph, Written Description

In the Office Action at pages 5-7, section 7, the Examiner has rejected claims 4, 5, 9, 12-16, 18 and 20 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

The Examiner contends the specification does not describe a sufficient number of species of DNA molecules encompassed by claims 4 and 5, alleging that the disclosure

of the complete complement of bases 87-1400 of SEQ ID NO:1, does not sufficiently describe the full genus of claimed complementary nucleic acid molecules. With regard to claim 9, the Examiner contends that claim 9 encompasses any protein encoded by the nucleic acid of claim 1, and hence, disclosure of only SEQ ID NO:2 is allegedly not representative of other proteins that have different structures and functions. The Examiner therefore concludes that the presently claimed invention does not comply with the written description requirement of 35 U.S.C. § 112, first paragraph. Applicants respectfully disagree with the Examiner's contentions and conclusions.

The Examiner relies on the Federal Circuit's decision in *University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997), for the proposition that the alleged disclosure of a single species of bases 87-1400 of SEQ ID NO:1, and its complete complement, does not provide a sufficient number of representative species of the genus of claims 4 and 5. Applicants note that *Capon v. Eshhar* clarifies the written description requirement as delineated by *Eli Lilly*. 418 F.3d 1349, 1358 (Fed Cir. 2005). In discussing the current state of the written description requirement under 35 U.S.C. §112, first paragraph, the Federal Circuit stated in *Capon*, "[s]ince the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field . . . ." *Capon*, 418 F.3d at 1358 (*emphasis added*). (*See also, Invitrogen Corp. v. Clontech Lab., Inc.*, 429 F.3d 1052, 1073 (Fed. Cir. 2005) holding that description of a single species is sufficient written description for claims directed to a modified polypeptide having DNA polymerase activity.)

Present claim 4 recites an isolated DNA that encodes a sense RNA comprising at least 15 nucleic acids that is at least about 90% complementary to, and hybridizes with, a nucleic acid molecule that is 100% complementary to the recited nucleic acid. Present claim 5 recites an isolated DNA that encodes an antisense RNA comprising at least 15 nucleic acids that is at least about 90% complementary to, and hybridizes with, the recited nucleic acid. As set forth above, the level of skill in the art at the time of filing must be taken into account when determining the level of disclosure necessary to meet the written description requirement. *See Capon,* 418 F.3d at 1358. Applicants respectfully submit that the disclosure of the nucleotide sequence encoding the MiLV protein, coupled with the level of skill in the art at the time of filing of the present application, provides sufficient written description of the presently claimed invention. A person of ordinary skill in the art, at the time of filing of the present application, would have readily understood that, given the nucleic acid sequence encoding the MiLV protein, Applicants clearly were in possession of a representative number of nucleic acid molecules encompassed by present claims 4 and 5.

Processes to generate RNA molecules with the recited complementarily, and methods for preparing DNA molecules encoding such RNA molecules, were all well known at the time of filing of the present application. Provided with a nucleic acid sequence (e.g., SEQ ID NO:1), a person of ordinary skill in the art could readily envision a large number of nucleic acid molecules that would have at least 90% complementarity to such a sequence, including sequences of greater than about 15 bases. A person of ordinary skill in the art would have been able to readily prepare nucleic acid molecules with the recited level of complementarity, as well as determine their ability to hybridize

with the nucleic acid molecules. Preparation of DNA molecules encoding these complementary nucleic acids would have also been well within the level of the ordinarily skilled artisan. Although the Examiner alleges that only a single species of the recited genus of complementary nucleic acids is disclosed, Applicants submit that a person of ordinary skill in the art would have readily been able to envision any number of complementary nucleic acid molecules, as well as the DNA molecules encoding them, when provided with the full length nucleic acid sequence of SEQ ID NO:1, in combination with the level of skill in the art at the time. Thus, the full scope of the presently claimed invention was in the possession of Applicants at the time of filing of the present application.

With regard to the Examiner's rejection of claim 9, present claim 9 recites an isolated Mirafiori lettuce virus coat protein having the amino acid sequence set forth in SEQ ID NO: 2. Applicants respectfully submit that this claim is clearly supported by the present specification, as the full amino acid sequence of SEQ ID NO:2 was provided in the sequence listing filed with the application. Thus, this claim clearly meets the written description requirement of 35 U.S.C. § 112, first paragraph.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, for alleged lack of written description.

The Rejection under 35 U.S.C. § 112, First Paragraph, Enablement

In the Office Action at pages 7-10, section 8, the Examiner has rejected claims 4, 5, 9, 12-16, 18 and 20 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The Examiner contends that, while the present specification enables a DNA encoding a sense RNA completely complementary to the completely complementary strand of bases 87-1400 of SEQ ID NO:1, or a DNA encoding an antisense RNA completely complementary to bases 87-1400 of SEQ ID NO:1, it allegedly does not enable other DNAs encompassed by claims 4 and 5. The Examiner contends that, as the term "complementary" is not limited to complete complementarity, DNAs encompassed by the claims can differ by any extent. In addition, the Examiner contends that the present specification does not provide any examples showing that DNAs of less than 23 nucleotides, having complete or incomplete complementarity to its target sequence, were able to silence expression of SEQ ID NO:1. The Examiner therefore concludes that the presently claimed invention is not enabled. Applicants respectfully disagree with the Examiner's contentions and conclusions.

As set forth in M.P.E.P. § 2164.01(a), there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the

invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, (Fed. Cir. 1988).

Applicants note, as discussed in detail above, the level of ordinary skill in the art of DNA/RNA preparation and sequencing at the time of filing was high. Furthermore, the state of the art at the time of filing of the present application was such that the ordinarily skilled artisan would have readily been able to prepare a large number of DNA molecules encoding complementary nucleic acids that would fall within the scope of present claims 4 and 5.

The present specification provides the nucleic acid sequence encoding the MiLV protein, in SEQ ID NO:1. Given this sequence, a person of ordinary skill in the art would have been able to produce numerous RNA molecules that were complementary to this sequence, including sequences that were 90-100% complementary, comprising at least 15 bases. The relationship between complementary nucleic acids (i.e., the ability to hybridize) was a well-known concept at the time of filing of the presently claimed invention, as were methods to produce RNA, and DNA molecules encoding such RNAs. Furthermore, assays to measure the ability of two RNA molecules to hybridize to one another were well known at the time of filing the present application.

Applicants respectfully submit that it clearly would not have required undue experimentation to prepare any number of DNA molecules encoding the complementary RNAs of present claims 4 and 5 using routine, well-known methods in the art. The Examiner is reminded that the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is *undue*. *See* M.P.E.P. § 2164.01 (*emphasis added*). Applicants submit that at most, only minor,

routine experimentation would be required to prepare the DNA molecules of the presently claimed invention.

The Examiner cites two references in support of the proposition that, RNAs of less than 23 nucleotides in length, do not act as silencers of targeted nucleic acids for use in antisense-based therapies. The Examiner thus concludes that, nucleic acids of 15 nucleotides, as disclosed in the present specification, are not enabled. Applicants respectfully disagree with the Examiner, and note that present claims 4 and 5 do not require that the recited RNAs be capable of inhibiting expression of the target protein. Rather, all that is required, in addition to the specified length and complementarity, is that the RNA hybridize with the recited RNA molecules. Thus, a person of ordinary skill in the art, guided by the present specification, would have been able to prepare numerous DNA molecules that encode the RNA molecules recited in present claims 4 and 5. While it may have required some experimentation to prepare the complementary RNA strands and the DNA molecules encoding such strands, this experimentation would have merely been routine. Thus, the presently claimed invention is clearly enabled.

With regard to the Examiner's rejection of claim 9, present claim 9 recites a Mirafiori lettuce virus coat protein having the amino acid sequence set forth in SEQ ID NO: 2. Applicants respectfully submit that this claim is clearly enabled, as the full amino acid sequence of SEQ ID NO:2 was provided in the sequence listing filed with the application. Thus, this claim clearly meets the enablement requirement of 35 U.S.C. § 112, first paragraph, as it would not have required any undue experimentation to produce this sequence, but rather, routine techniques and methods, as detailed in the present specification.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, for alleged non-enablement.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, rendered moot or otherwise overcome. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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